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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/565,283	04/20/2006	Teruo Sugawara	472325006	5242

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EXAMINER	
LONG, SCOTT	

ART UNIT	PAPER NUMBER
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/565,283	SUGAWARA, TERUO	
	Examiner	Art Unit	
	Scott D. Long	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 October 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/22/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

Claims 1-4 are pending. Claims 1-4 are under current examination.

Sequence Compliance

Sequence Listing and CRF have been received and are acknowledged by examiner. A statement that the Computer Readable Form (CRF) and the Sequence Listing are identical has been submitted and is acknowledged by examiner.

Oath/Declaration

The oath or declaration, having the signatures of all inventors, received on 20 April 2006 is in compliance with 37 CFR 1.63.

Information Disclosure Statement

The Information Disclosure Statements (IDS) filed on 22 February 2007 consisting of 1 sheets are in compliance with 37 CFR 1.97. Accordingly, examiner has considered the Information Disclosure Statements.

Priority

This application claims as a 371 of PCT/JP04/03449 (filed 03/15/2004). This application also claims benefit from foreign application, JAPAN 2003278429 (filed 07/23/2003). Since no English translation of the foreign application has been submitted, the benefit has not been perfected. Therefore, the instant application has been granted the benefit date, 13 March 2004, from the application PCT/JP04/03449

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1-2 are drawn to RNA molecules, that are identical to portions of SEQ IDNO:1, which is a DNA sequence. The contradiction between types of nucleic acids makes these claims unclear. Likewise, the kit and method of claims 3-4 are also unclear because they comprise the nucleic acids of claims 1-2. Clarification of this issue is required.

Furthermore, claims 1-2 are not drawn to isolated oligoribonucleotides. Because small RNAs are found in nature, the language of the instant claims is unclear and possibly non-statutory. Clarification is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for in vitro method for inhibiting expression of SBP in cancer cells, does not reasonably provide enablement for in vivo methods for inhibiting expression of SBP in cancer cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in *Wands* states: "Enablement is not precluded by the necessity for some 'experimentation.'" Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the

breadth of the claims. While all of these factors are considered, a sufficient amount for a prima facie case is discussed below.

SCOPE OF THE INVENTION

In the instant case, claim 3 is directed to methods of gene therapy comprising delivery of small RNA molecules both cells and living organism. The specification suggests that the oligoribonucleotides of the instant invention could be used as a cancer treatment (page 1,lines 16-26). Implicitly, the intended use of these products and methods are for gene therapy. However, there is insufficient support in the specification for gene therapy applications in vivo.

In addition, claim 4 is directed to a kit for cancer therapy. However, the specification does not elaborate on how the constituents of the kit are actually utilized therapeutically to reduce a tumor, for example.

GUIDANCE & WORKING EXAMPLES

The specification suggests that the oligoribonucleotides of the instant invention could be used as a cancer treatment (page 1,lines 16-26). Implicitly, the intended use of these products and methods are for gene therapy. However, there are no working examples that demonstrate gene therapy applications in vivo.

In addition, the specification does not elaborate on how the constituents of the kit are actually utilized therapeutically. All of the working examples involve cell culture

experiments; none of the working examples demonstrate the use of the kit as a cancer therapy on a whole organism.

In addition, Claims 3-4 utilize oligoribonucleotides of claims 1-2 that are based on nucleotides 474-494 of SEQ ID NO:1. However, no oligoribonucleotide which has this sequence was utilized in the *in vitro* experiments described in the instant application. In fact, Example 6 (page 11), utilizes SEQ ID NO:6-7, but these oligoribonucleotides do not match 474-494 of SEQ ID NO:1. There is a one base difference at base 492 of SEQ ID NO:1; the DNA sequence is a cytosine, while the RNA is a guanine. Therefore the example does not demonstrate a method of inhibiting expression of SBP gene in cancer cells utilizing oligoribonucleotides of claims 1-2 that are based on nucleotides 474-494 of SEQ ID NO:1.

The absence of working examples directed to in vivo methods necessitates further experimentation. Therefore, the specification does not provide sufficient guidance on how to make and use in vivo methods of inhibiting expression of SBP gene in cancer cells or the use of the kit for cancer therapy.

STATE OF THE ART & QUANTITY OF EXPERIMENTATION

In view of the state of the art and the level of the skilled in gene therapy art, it is still under development and highly unpredictable. *Orkin et al.* (NIH Report, 1995 Dec) reviews the infant state of the art of gene therapy from before the instant invention was made. The overall conclusions were: 1) gene therapy for each disease would present its own scientific and clinical challenges; 2) no successful gene therapy protocol was

known; 3) significant problems remained in all aspects of gene therapy, especially with respect to effective expression vectors; 4) one cannot predictably extrapolate the result of one animal model, such as mouse, to treatment of a disease in a different animal, such as human; and 6) assessment of known gene therapy protocols was hindered by poor gene transfer, reliance on qualitative, rather than quantitative assessments of gene transfer, lack of suitable controls and poor definition of biochemical or disease endpoints (pages 1-2). Although the reference is from a few years before the foreign application (JAPAN 2003278429), the general status of gene therapy art has not significantly changed. *Patterson* (STATEMENT OF AMY PATTERSON M.D., February 2000) reviews "THE SUCCESS OF THIS TECHNOLOGY [GENE THERAPY] IS DEPENDENT UPON NOT ONLY THE DELIVERY OF GENETIC MATERIAL INTO THE TARGET CELLS, BUT ALSO THE EXPRESSION OF THE GENE ONCE IT REACHES ITS TARGET SITE. BOTH OF THESE REQUIREMENTS POSE CONSIDERABLE TECHNICAL CHALLENGES". *Patterson* further teaches that out of 372 clinical trials registered with the NIH, only one percent of the trials (3) have progressed to Phase III efficacy studies. "FOR THIS REASON, IT IS PERHAPS MORE ACCURATE TO REFER TO THIS TECHNOLOGY AS 'GENE TRANSFER', RATHER THAN 'GENE THERAPY', UNTIL THERE IS MORE EVIDENCE FOR THE THERAPEUTIC BENEFIT OF THIS TECHNOLOGY".

In a review entitled "Antisense Oligonucleotide Drug Design," Schiavone et al. (2004) concludes that "Despite promising futures, antisense-based therapeutics are far from being an established reality."(see Abstract). Moreover, Schiavone et al. further state: "[A]lthough the antisense approach is an attractive and promising field for both molecular biology research and the pharmaceutical industry, it also involves unwanted,

or even toxic, non-antisense effects and is controversial about its actual specificity. As to the specificity, at least two conditions must be satisfied to guarantee that the phenotypic effect of an antisense is actually restricted to its sequence-specific annealing with the targeted mRNA: (1) the level of the targeted RNA and relevant protein must decrease significantly, but (2) the level of at least another unrelated mRNA and relevant protein used as control (generally a constitutive protein, such as beta-actin or alpha-globin) must remain unaffected."

The instant application does not overcome the difficulties intrinsic to antisense gene therapy treatments of Cancer using StAR-binding protein. Consequently, there is ample reason to conclude that there would be a high degree of unpredictability in a mammalian embodiment of the instant invention.

CONCLUSION

In conclusion, given the breadth of the claims and the limited scope of the specification, an undue quantity of experimentation is require to make and use the invention beyond the scope of use in vivo methods of inhibiting expression of SBP gene in cancer cells or the use of the kit for cancer therapy. In addition, claim 3 is further limited to *in vitro* methods of inhibiting expression of SBP gene in cancer cells utilizing oligoribonucleotides of claims 1-2 that are based on nucleotides 187-205 of SEQ ID NO:1.

Conclusion

No claims are allowed.

Examiner Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**. The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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